MAIL STOP APPEAL BRIEF-PATENTS
PATENT
2503-1215

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of

Ezio BOMBARDELLI — Conf. 1808

Application No. 10/580,190 — Group 1655

Filed May 23, 2006 — Examiner Qiuwen Mi

COMPOSITIONS FOR THE TREATMENT OF AFFECTIONS OF THE ORAL CAVITY AND UPPER RESPIRATORY TRACT

APPEAL BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

MAY IT PLEASE YOUR HONORS:

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1. Real Party in Interest

THE REAL PARTY IN INTEREST IN THIS APPEAL IS:

INDENA S.P.A., VIALE ORTLES 12, I-20139 MILANO, ITALY.

2. Related Appeals and Interferences

NONE.

3. Status of Claims

Claims 2-5 and 16 have been canceled. Claims 1, 6-15 and 17-25 are pending in the application and stand rejected, from which this appeal is taken.

4. Status of Amendments

No amendments have been filed subsequent to the final rejection mailed August 27, 2009. The claims at issue are thus those set forth in the Amendment filed May 4, 2009.

5. Summary of Claimed Subject Matter

Independent claim 1: As is set forth in independent claim 1, the present invention pertains to compositions that include:

a) anthocyanosides, procyanidins and phloroglucinols;

b) anthocyanosides and phloroglucinols; and

c) procyanidins and phloroglucinols (Page 1, lines 14-17), for the treatment of the affections of the oral cavity and upper respiratory tract (Page 1, lines 18-19), wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract (Page 1, lines 24-25),

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins (page 2, lines 8-11), and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts (page 2, lines 16-19) , and wherein the compositions contain at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols (Page 1, lines 20-22).

Independent claim 15: As is set forth in independent claim 15, the present invention pertains to a method for the preparation of a medicament for treatment of affections of the oral cavity and upper respiratory tract (Page 4, lines 4-8), which includes:

administering to a patient in need thereof an effective amount of a medicament containing (Page 1, lines 5-12):

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; and

c) procyanidins and phloroglucinols (Page 1, lines 14-17), wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract (Page 1, lines 24-25),

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins (page 2, lines 8-11), and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts (page 2, lines 16-18),

and wherein the medicament contains at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols (Page 1, lines 20-22).

Independent claim 24: As is set forth in the independent claim 24, the present invention pertains to compositions which include:

b) anthocyanosides and phloroglucinols; and

c) procyanidins and phloroglucinols (Page 1, lines 16-17), for the treatment of the affections of the oral cavity and upper respiratory tract(Page 1, lines 18-19) , wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract(Page 1, lines 24-25),

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins (page 2, lines 8-11), and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts (page 2, lines 16-18),

and wherein the compositions contain at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols (Page 1, lines 20-22).

Independent claim 25: as is set forth in independent claim 25, the present invention pertains to a method for the preparation of a medicament for treatment of affections of the oral cavity and upper respiratory tract (page 4, lines 4-8), which includes:

administering to a patient in need thereof an effective amount of a medicament containing as active principle (page 1, lines 5-12):

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; and

c) procyanidins and phloroglucinols (Page 1, lines 15-17), wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract (Page 1, lines 24-25),

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins (page 2, lines 8-11), and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts (page 2, lines 16-18),

and wherein the medicament contains at least one of:

the anthocyanosides, the procyanidins or the phloroglucinols in an amount effective to induce synergy (Page 3, lines 7-9).

6. Grounds of Rejection to be Reviewed on Appeal

The first ground for review on appeal is whether claims 1, 6-15 and 17-25 are unpatentable under 35 U.S.C. §112, first paragraph, as being failing to comply with the written description requirement.

The second ground for review on appeal is whether claims 1, 7, 8, 15, 18 and 19 are sufficiently unpatentable over YALOVENY AGRIC IND (SU 1373398A), as evidenced by NIEUWENHUIZEN et al. (US 2003/0064937) and COOPER et al. (US 6,379,720), in order to support an allegation of unpatentability under 35 U.S.C. §103.

The third ground for review on appeal is whether claims 1, and 6-15, and 17-25 are sufficiently unpatentable over WALKER et al. (US 5,474,774), IMAOKA et al. (JP 06179609 A), BARNEY et al. (US 5,370,863), VAN DEN BERGHE (US 6,284,289), and ZOU (CN 1421240), as evidenced by GORENBEIN et al. (US 5,955,102), NIEUWENHUIZEN et al., COOPER et al., GHOSAL (US 6,224,906), APPENDINO et al. (Oligomeric acylphloroglucinols from myrtle (*Myrtle communis*) and Journal of Natural Products, 65 (3): 334-8,2002), in order to support an allegation of unpatentability under 35 U.S.C. §103.

7. Argument

7.0 Summary of Argument

The claimed compositions for treating oral affections of the oral cavity and upper respiratory tract are supported and patentable over the applied art. The unexpected results are commensurate in scope with the claims and therefore dissipate any unpatenatbility that could be alleged.

7.1 First Ground - Written Description

Claims 1, 15 and 24 recite "100 mg of the anthocyanosides, 100 mg of the procyanidins, or 100 mg of the phloroglucinols." The Office asserts that there is no support for the "100 mg" limitations.

However, page 1, lines 20-22 of the specification teaches 1 to 200 mg of the anthocyanosides, 1 to 200 mg of the procyanidins, and 1 to 200 of the phloroglucinols. The 100 mg limitation (although not explicitly stated) is clearly within the 1 to 200 mg range.

The propriety of the "100 mg" limitations is clearly supported by case law.

For example, in *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of "25% - 60%" and specific examples of "36%" and "50%." A corresponding new claim limitation to "at least 35%" did not meet the description requirement because the phrase "at least" had no upper limit and caused the claim to read literally on embodiments outside

the "25% to 60%" range, however a limitation to "between 35% and 60%" did meet the description requirement.

Therefore, a value within a range is proper even if it is not explicitly set forth in the specification.

Withdrawal of this rejection is accordingly indicated.

7.2 Second Ground - Rejection Over YALOVENY AGRIC IND, NIEUWENHUIZEN et al. and COOPER et al.

The present invention pertains to compositions for treatment of affections of the oral cavity and upper respiratory tract, containing:

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; ***or***

c) procyanidins and phloroglucinols.

As is set forth in independent claims 1 and 15 of the present invention: "the anthocyanosides are derived from *Vaccinium myrtillus* extract, the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing them, and the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts." Independent claims 1 and 15 also set forth that the compositions contain at least one of: 100 mg of the anthocyanosides, 100 mg of the procyanidins, or 100 mg of the phloroglucinols.

YALOVENY AGRIC IND pertains to non-alcoholic drinks containing grape juice, wine grape seeds, wine-spirit extract of hops, lemon oil, carbon dioxide and water. YALOVENY AGRIC IND fails to disclose compositions for treatment of affections of the oral cavity and upper respiratory tract, such as are set forth in claims 1, 15 and 24 of the present invention. The soft drinks of YALOVENY AGRIC IND also represent non-analogous art.

NIEUWENHUIZEN et al. pertain to a composition for reducing appetite in mammals. NIEUWENHUIZEN et al. at, e.g., paragraph 23 discuss that procyanidins are obtained from a plant source such as grape seed.

COOPER et al. pertain to compositions containing hops extract and their use in water systems and process streams to control biological fouling. Column 1, lines 50-58 of COOPER et al. include a discussion of alpha acids such as cohumulone and adlupulone. However, COOPER et al. fails to mention phloroglucinol.

All three of YALOVENY AGRIC IND, NIEUWENHUIZEN et al. and COOPER et al. fail to disclose compositions for treatment of affections of the oral cavity and upper respiratory tract, such as are set forth in claims 1 and 15 of the present invention. These references particularly do not disclose or infer the “100 mg” limitation of the independent claims.

One of ordinary skill would accordingly fail to produce claims 1 and 15 of the present invention from a knowledge of YALOVENY AGRIC IND, NIEUWENHUIZEN et al. and COOPER et al., and a *prima facie* case of unpatentability has thus not been made.

Moreover, a Declaration demonstrating unexpected results has been made of record in the application (see attachment).

The Declaration set forth experimental results that were found to be convincing in the written opinion issued by the EPO. The Declaration set forth the experimentation reproduced below.

Six groups of 20 patients of both sexes suffering from acute bacterial pharyngitis and throat pain were enrolled.

The patients were treated with ***100 mg*** of the single active principle (either anthocyanosides, procyanidins or floroglucinol) three times a day for 3 days.

Before and at 60 min after the last treatment the patients were asked to assess pain intensity (P.I) according to the following 6-point (0-5) scale:

0 = no pain,

1= hardly any pain,

2 = moderate pain,

3 = moderately severe pain,

4 = severe pain,

5 = very severe pain.

Moreover, hyperaemia of pharynx and tonsils was also evaluated according to a 4-point scale (absent = 0, slight = 1, moderate = 2, severe 3). The results are reported in Table 1.

TABLE 1

	P.I.		**Inflammation of pharynx and tonsils**	
	Basal Value	**After treatment**	**Basal Value**	**After treatment**
Vaccinium myrtillus extract (A)	4.7	4.0	2.8	1.9
Vitus vinefera extract (B)	4.5	4.1	2.8	2.0
Mirtus Communis extract (C)	4.6	4.2	2.9	2.2
Composition containing B+C	4.6	2.5	2.8	0.7
Composition containing A+B+C	4.7	1.7	2.9	0.1
Placebo	4.6	4.4	2.9	2.8

At the same time, the patients proceeded with a 20s gargling with 10 ml sterile distilled water followed by the collection of samples.

The samples were adequately diluted with Ringer's solution containing 0.2% dithiothreitol, and 0.5 ml of each dilution were spread on 4 agar plates (Columbia) supplemented with 5% sheep blood. The plates were incubated in a CO_2 atmosphere for 72 h for anaerobic culture. After incubation the number of colonies was counted. The results are reported in Table 2.

TABLE 2

	Bacterial count ($x10^5$) in gargling samples	
	Basal Value	**After treatment**
Vaccinium myrtillus extract (A)	20.2	15.2
Vitus vinefera extract (B)	21.4	16.9
Mirtus Communis extract (C)	21.0	17.2
Composition containing B+C	23.2	4.9
Composition containing A+B+C	22.9	2.6
Placebo	23.6	22.4

It should be noted that the experiments reported in the Declaration were carried out using dosages of ***100 mg*** each. The Declaration provides convincing evidence that the three compounds in a 1:1:1 ratio by weight have synergistic effects. It is logical that only the weight ratio is critical for synergy whereas the actually selected dosage may depend upon the patient's weight and sex as well as on other factors. It

does not accordingly seem logical to exclude from the claims dosages ranging in the same order of magnitude, such as 110, 150, 180 mg etc.

The results set forth in the Declaration are accordingly commensurate in scope with the claims. Any unpatentability that may be alleged over the applied art is thus dissipated by the unexpected results.

Withdrawal of this rejection is accordingly indicated.

7.3 - Third Ground - IMAOKA et al. BARNEY et al., VAN DEN BERGHE, ZOU, GORENBEIN et al., NIEUWENHUIZEN et al., COOPER et al., GHOSAL, and APPENDINO et al.

IMAOKA et al. pertain to a composition for oral cavity applications that contains grape extract.

BARNEY et al. pertain to oral care compositions containing hop acids. BARNEY et al. fail to teach or suggest the utilization of pure phloroglucinols from *Humulus* extracts. BARNEY et al. additionally fail to teach or suggest combining hops acids with other ingredients.

VAN DEN BERGHE pertains to treating herpes with a quaternary ammonium compound. *Myrtus communis* and *Hypericum perforatum* are cited in a long list of plants used as additional ingredients of the composition. There is no hint whatsoever that would have led a skilled person to select these two specific ingredients and to combine them with

procyanidins derived from a *Vitis vinifera* extract or a *Camillia sinensis* extract.

ZOU pertains to mint oil. Mint oil and derivatives thereof are not contained in the compositions of the present invention, and therefore a skilled person would not have considered this document as a relevant source of information. ZOU is thus non-analogous art.

NIEUWENHUIZEN et al. at, e.g., paragraph 23 discuss that procyanidins are obtained from a plant source such as grape seed.

GORENBEIN et al. is used for teachings pertaining to bilberry extract. GHOSAL is used for teachings pertaining to St. John's wort. Appendino et al. is used for teachings pertaining to the phloroglucinal contained in *Myrtus communis*.

However, combining this multiplicity of references strongly infers impermissible hindsight reconstruction.

Even if for the sake of argument these references could be combined to produce what would clearly be a weak *prima facie* case of unpatentability, this unpatenability would be dissipated by the unexpected results, especially in regards to the "100 mg" recitations.

This rejection should accordingly be withdrawn.

7.4 Statement of Substance of Interview

The Examiner is thanked for graciously conducting a telephonic interview with the appellant's representative on August 21, 2009. During the interview the patentability of the present invention was discussed, along with potential amendments to the claims. Agreement was not reached.

At the end of the interview the Examiner prepared an interview summary. The interview summary has been reviewed, and it appears to accurately reflect the substance of the interview.

8. Conclusion

The Appellant has demonstrated that the Examiner has failed to successfully allege that the rejected claims are new matter or *prima facie* unpatentable. It is clear that the inventive compositions for treatment of affections of the oral cavity and upper respiratory tract represent a truly inventive technology, as is evidenced by the unexpected results. For the reasons advanced above, it is respectfully submitted that all the rejected claims in this application are allowable. Thus, favorable reconsideration and reversal of the rejections of the under 35 USC §§112/103, by the Honorable Board of Patent Appeals and Interferences, are respectfully solicited.

Please charge the requisite Appeal Brief fee in the amount of $540 to our credit card.

Respectfully submitted,

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9. Claims Appendix

1. Compositions comprising:

a) anthocyanosides, procyanidins and phloroglucinols;

b) anthocyanosides and phloroglucinols; and

c) procyanidins and phloroglucinols, for the treatment of the affections of the oral cavity and upper respiratory tract, wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract,

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins, and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts,

and wherein the compositions contain at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols.

6. The compositions as claimed in claim 1, wherein the phloroglucinols are derived from *Hypericum perforatum* or *Myrtus communis* extracts, or from *Humulus lupulus* fractions enriched in α and β acids.

7. The compositions as claimed in claim 6, wherein the β acids fraction from *Humulus lupulus* contains 20 to 80% of phloroglucinols expressed as colupulone, and the α acids contains 20 to 80% of humulone.

8. The compositions as claimed in claim 7, wherein the β acids fraction prepared from *Humulus lupulus* contains 60% of phloroglucinols expressed as colupulone, and the α acids contains 60% of humulone.

9. The compositions as claimed in claim 1, wherein the *Hypericum sp.* extracts include a *Hypericum perforatum* extract with a phloroglucinols content ranging from 20 to 80%.

10. The compositions as claimed in claim 9, wherein the phloroglucinols content of the *Hypericum perforatum* extract is 60%.

11. The compositions as claimed in claim 6, wherein the *Myrtus communis* extract is prepared from leaves of *Myrtus communis* by extraction with carbon dioxide under conditions of pressure ranging from 235 to 260 bars and temperatures ranging from 40 to 60°C.

12. The compositions as claimed in claim 11, wherein the *Myrtus communis* extract has a content in myrtucommulone of 35%.

13. The compositions as claimed in claim 1, further containing at least one essential oil.

14. The compositions as claimed in claim 13, wherein the essential oil is mint oil.

15. A method for the preparation of a medicament for treatment of affections of the oral cavity and upper respiratory tract, which comprises:

administering to a patient in need thereof an effective amount of a medicament containing:

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; and

c) procyanidins and phloroglucinols, wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract,

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins, and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts,

and wherein the medicament contains at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols.

17. The method as claimed in claim 15, wherein the phloroglucinols are derived from *Hypericum perforatum* or *Myrtus communis* extracts, or from *Humulus lupulus* fractions enriched in α and β acids.

18. The method as claimed in claim 17, wherein the β acids fraction from *Humulus lupulus* contains 20 to 80% of phloroglucinols expressed as colupulone, and the α acids contains 20 to 80% of humulone.

19. The method as claimed in claim 18, wherein the β acids prepared from *Humulus lupulus* contains 60% of phloroglucinols expressed as colupulone, and the α acids fraction contains 60% of humulone.

20. The method as claimed in claim 1, wherein the *Hypericum sp.* extract is a *Hypericum perforatum* extract with phloroglucinols content ranging from 20 to 80%.

21. The method as claimed in claim 20, wherein the phloroglucinols content of the *Hypericum perforatum* extract is 60%.

22. The method as claimed in claim 17, wherein the *Myrtus communis* extract is prepared from leaves of *Myrtus communis* by extraction with carbon dioxide under conditions of pressure ranging from 235 to 260 bars and temperatures ranging from 40 to 60°C.

23. The method as claimed in claim 17, wherein the *Myrtus communis* extract has a content in myrtucommulone of 35%.

24. Compositions comprising:

b) anthocyanosides and phloroglucinols; and

c) procyanidins and phloroglucinols, for the treatment of the affections of the oral cavity and upper respiratory tract, wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract,

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins, and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts,

and wherein the compositions contain at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols.

25. A method for the preparation of a medicament for treatment of affections of the oral cavity and upper respiratory tract, which comprises:

administering to a patient in need thereof an effective amount of a medicament containing as active principle:

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; and

c) procyanidins and phloroglucinols, wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract,

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins, and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts,

and wherein the medicament contains at least one of:

the anthocyanosides, the procyanidins or the phloroglucinols in an amount effective to induce synergy.

10. Evidence Appendix

An executed Declaration under 37 C.F.R. §1.132, filed on May 7, and made of record in the Final Office Action of May 30, 2008.

11. Related Proceedings Appendix

NONE.